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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/885,679	PERA, MARTIN FREDERICK	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-56,59-65 and 68-83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *50-56 and 69-79* is/are allowed.

6)☐ Claim(s) *80-83* is/are rejected.

7)☒ Claim(s) *59-65 and 68* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

8.0.0

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 28, 2005 has been entered.

DETAILED ACTION

This application filed June 20, 2001 claims benefit to foreign applications PR1327, filed November 8, 2000, and PQ8242, filed June 20, 2000, both in Australia.

Applicants' amendment filed April 28, 2005, has been received and entered. The abstract of the specification has been amended. Claims 1-49, 57, 58, 66 and 67 have been canceled. Claims 50-56, 60-65 have been amended. Claims 68-83 have been added. Claims 50-56, 59-65 and 68-83 are pending.

It was noted that upon review of the electronic file that a summary of the personal interview conducted April 21, 2005 was not scanned nor entered. A copy of the interview summary is included with this action for Applicant's records.

Election/Restriction

Applicant's election with traverse of group I, and the election of species of noggin in Paper No. 11 was acknowledged. The requirement was deemed proper and made FINAL. No new grounds of traversal have been provided.

Upon re-consideration of the claimed subject matter, the election of species is withdrawn.

Claims 50-56, 59-65 and 68-73 are pending and currently under examination as they are drawn to methods of culturing ES cells with a BMP antagonist.

Specification

The abstract of the disclosure objected to because it is not present as a single paragraph is withdrawn.

As indicated in Applicants' remarks (page 7), a corrected abstract was received December 8, 2003, and is in compliance with the guidelines of MPEP 608.01(b)

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over copending Application No. 09/670,198 is withdrawn.

As indicated in Applicants' comments (page 9), application 09/670,198 has been abandoned.

With respect to Applicants' comments regarding pending application 10/616,682, (pages 9-12) Examiner agrees that the pending claims in each application are directed to two different patentably distinct inventions.

It is noted that a review of other pending applications by the inventor identifies related subject matter encompassing broadly claimed methods of obtaining, culturing, and differentiating stem cells, however presently none of the pending claims specifically claim the use of antagonists of the BMP pathway. Application 11/049,830 is the closest in claimed subject matter in methods of obtaining neural stem cells, however a cursory review of the specification

does not provide the guidance to use antagonist of BMP, or more specifically noggin in methods of differentiation to obtain neural stem cells and rely instead appear to rely on factors and methods known in the prior art.

Newly amended claims 59-65 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 50-56. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

In a comparison of the amended claims the claim sets appear to be duplicates of each other. Examiner can not find a difference in the breadth between the two sets of claims.

Claim Rejections - 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 50-56, 59-65 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of culturing human embryonic stem (ES) cells comprising: (1) obtaining a source of human ES cells; and (2) providing culturing conditions of said human ES cells in the presence of noggin for 5 days wherein said conditions result in an undifferentiated cell which does not express ES stem cell markers, does not reasonably provide enablement for methods for producing progenitor cells is withdrawn.

Applicant argues that the present specification provides adequate guidance to practice the breadth of the method as claimed (pages 12-13), and that the further characterization of the resulting cell was an effort to delineate the identification of the intermediate cell that resulted in practicing the methodology (pages 13-14).

As stated previously Examiner would agree that the ability of the resulting cell to differentiate into neuronal cell types is consistent with the activity previously known and described for noggin and BMP-2. Cited art by Gratsch *et al.* and Carpenter *et al.* provide evidence that noggin is a neurotrophic factor and in the characterization of recombinant human noggin, at the time of filing, was known in the art to be a neurogenic factor affecting BMP-2 and was important in neuronal differentiation. Examiner did not contend that the one could not simply culture cells with noggin or other antagonists of the BMP pathway, nor that prolonged culturing with such factors would ultimately result in the formation of cells of neuronal cell lineages as this is supported by the art of record. To the extent that claims have been amended to encompass methods of making neural progenitor cells, Examiner agrees that the specification provides evidence that the noggin treated human ES cell are capable of differentiating into neuronal and glial cells, and that the resulting noggin treated human ES cell can be used for a facile route to the isolation of neuronal progenitors (page 29, lines 13-14). Further, Examiner has acknowledged that the methods provide for a cell that lacks neuronal markers and lacks stem cell markers as well, and that the noggin treated cell appears to be an intermediate cell type. Again, this is not generally unexpected because the culturing of an undifferentiated cell into a differentiated cell must proceed through the process of differentiation providing intermediate cell types or at least phenotypes not representative of either a completely undifferentiated or

differentiated cell type. Based on the affect of noggin, there is no evidence of record that this affect would not extend to other BMP pathway antagonists.

With respect to the cell that is produced, clearly the evidence of record indicates that the resulting cell is no longer an ES cell nor is it a neural progenitor cell. Clearly the methods can be practiced, and the evidence of record indicates that the resulting cell is intermediate to the ES cell and other lineage specific stem cells as evidenced by the presence/absence of cells surface markers conventionally used in the art to define a specific cell type. Given the evidence of record and in view of the specific claim language now set forth in the pending claims, Examiner agrees that the methods are fully enabled.

Claim Rejections - 35 USC ∋ 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 57, 58, 66 and 67 rejected under 35 U.S.C. 102(b) as being anticipated by Thomson (US Patent 5,843,780) is moot in light of their cancellation.

Claims 57, 58, 66 and 67 rejected under 35 U.S.C. 102(e) as being anticipated by Carpenter *et al.* (Pub. No. US2002/0019046 A1) is moot in light of their cancellation.

Claims 80-83 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomson (US Patent 5,843,780) or Carpenter *et al.* (Pub. No. US2002/0019046 A1).

The specification does not specifically define a progenitor cell however within the context of the methods the term is described as a cell which is capable of differentiation into any somatic lineage (page 14, lines 24-26). As noted previously given the guidance of the specification used to interpret the metes and bounds of the claims, they can reasonably be interpreted to broadly encompass any progenitor cell made by any method. With respect to claims 80 and 82, no specific characteristic of the resulting cell is set forth in the product claims and further, there is no guidance nor support in the specification for which cell marker would define this change from stem cell to progenitor cell. The claim is being given its broadest most reasonable interpretation in light of the teachings of the specification and the art of record. The term "progenitor cell" as recognized in the art is a general term which is consistent with that set forth in the specification as cited above, and for the purposes of art rejections is being interpreted by the functional ability of the cell to give rise to any somatic cell lineage. In this case, because embryonic stem cells are capable of giving rise to any somatic cell lineage, an ES cell can be interpreted to be a type of progenitor cell. With respect to claims 81 and 83, the evidence of record indicates that ES cells do not have any of these specific markers recited in the claims.

Thomson teach primate embryonic stem cells. The stem cells are pluripotent capable of giving rise to the various somatic cell lineages which is demonstrated by injecting the cells into a

SCID mouse and analyzing the resulting cell types (column 11, lines 12-58). With respect to the specific antibody markers, it is noted that Thomson does not specifically analyze for the presence or absence of these cell surface markers, however as recognized in the art and indicated in the present specification they represent markers on ES cell cultures which are allowed to spontaneously differentiate and are present at early time points of 7-10 days in culture (page 13, lines 20-30). Because the primate ES cells described by Thomson are highly pluripotent and not subject to differentiating conditions in culture, they would not have any of these cell surface markers. Similarly, Carpenter *et al.* teach primate pluripotent stem cells, and specifically teach that embryonic stem cells as taught by Thomson (page 4, paragraphs 45-48, in particular paragraph 46). Thus, to the extent that the instantly claimed products encompass pluripotential embryonic stem cells, Carpenter *et al.* anticipate the claims.

Again because the resulting cells are not fully describe in the present specification, and claimed as a product by process where, as here, the claimed and prior art products are identical or substantially identical, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw,* 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown,* 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). With respect to the methods wherein the ES cells are cultured in the presence of noggin or where noggin is used to produce a progenitor cell, any particular affect of these methods on the ES or resulting progenitor cell to differentiate from that known in

the art is not set forth. Therefore in this case, the undifferentiated ES cells and progenitor cells being claimed are being interpreted to be cells defined by their functional properties which are cells capable of giving rise to any cell type of any lineage. As noted above, Thomson teach that the primate embyronic stem cells are pluripotent and capable of giving rise to the various somatic cell lineages which was demonstrated by injecting the ES cells into a SCID mouse and analyzing the resulting cell types (column 11, lines 12-58). Since the ES cells described by Thomson have the phenotypic characteristics of ES/progenitor cells recognized in the art as defined and supported by the instant specification, the primate ES cells described by Thomson anticipate the instantly claimed ES/progenitor cells which were cultured in the presence of noggin.

Importantly, the present specification acknowledges that even the specific cell type produced in the working example has not fully characterized. Given the limited disclosure of the cells produced by the claimed methods and the breadth of the types of cells encompassed by the terms as recognized in the art, it is maintained that the cells taught by Thomson anticipate the instantly claimed cells.

Conclusion

Claims 50-56, 69-79 are allowed. Claim 68 is objected to because is dependent on rejected claim 59.

Based on the art of record, the present disclosure is the first to propose the use of antagonists of the BMP pathway, and reduce to practice methods that demonstrate that the use of such agonists result in possibly a more directed lineage differentiation of an embryonic stem cell.

Methods setting forth the generation of neural stem cells are clearly enabled as evidenced by the working examples, and the methods encompassing a less differentiated progenitor cell are considered enabled because of evidence of record, and the requirement that the differentiation pathway would require the production of intermediate cell types during the process of practicing the methods as claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

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